New method shrinks metastatic ovarian cancer and reduces chemotherapy dose

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New research published in the February 2015 issue of *The FASEB Journal*, may eventually help improve the five-year survival rate of ovarian cancer patients by describing a new way of shrinking ovarian cancer tumors while also simultaneously improving drug delivery. This new method involves the use of a portion of a naturally occurring protein inhibitor of angiogenesis called thrombospondin-1 or TSP-1. The portion, known as 3TSR, interacts with another protein called CD36 causing cells needed for tumors to create new blood vessels (endothelial cells) to stop growing and die. In turn, this reduces the formation of new blood vessels (angiogenesis) needed for tumors to grow.

"We hope that this study will lead to novel treatment approaches for women diagnosed with advanced stage ovarian cancer," said Jim Petrik, Ph.D., a researcher involved in the work from the Department of Biomedical Sciences at the University of Guelph in Guelph, Ontario. "The use of anti-angiogenic therapy, combined with metronomic chemotherapy, has the potential to significantly improve our ability to treat advanced stage ovarian cancer while simultaneously reducing the treatment effects for women diagnosed with this disease."

To make their discovery, Petrik and colleagues injected mouse ovarian cancer cells into the ovaries of mice. The resulting tumors were allowed to grow until they were similar to those in patients with advanced ovarian cancer, including the spread of small tumors throughout the abdomen. Pre-treatment with 3TSR improved chemotherapy drug delivery and when combined with low-dose chemotherapy, resulted in the most significant tumor regression and survival. This approach caused tumor shrinkage and resulted in destruction of abnormal, dysfunctional tumor blood vessels. The result was a smaller tumor, with improved blood supply. Researchers were then able to exploit this enhanced blood supply to improve chemotherapy drug delivery to the tumor and were able to treat with very small amounts of drug, with excellent clinical effect.

"When Judah Folkman first proposed the idea that tumor growth depended on angiogenesis," said Gerald Weissmann, M.D., Editor-in-Chief of *The FASEB Journal*, "he was dismissed by his peers. Now, of course, it's a given fact and this new work extends the concept. It shows that biologically-based inhibitors of angiogenesis work together with chemotherapy to bring us closer to tumor cures than ever before."

More information: Samantha Russell, Mark Duquette, Joyce Liu, Ronny Drapkin, Jack Lawler, and Jim Petrik. Combined therapy with thrombospondin-1 type I repeats (3TSR) and chemotherapy induces regression and significantly improves survival in a preclinical model of advanced stage epithelial ovarian cancer. *FASEB J*. February 2015 29:576-588; DOI: 10.1096/fj.14-261636

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